REMARKS

The present application contains 27 claims, among which Claims 12-20 and 26 are rejected, and Claims 1-11, 21-25 and 27 are withdrawn from consideration due to the Restriction Requirement of March 6, 2005.

Applicants acknowledge with thanks the Examiner's statement that Claims 16, 19 and 20 would be allowable if rewritten to overcome the rejection under 35 U.S.C. §112, second paragraph, and if rewritten in independent form to include all of the limitations of the base claim and any intervening claims. However, applicants respectfully decline the Examiner's suggestion for the reasons discussed below.

Before addressing the merits of the rejections raised in the present Office Action, applicants have amended Claims 12-14 to recite proper Markush format. Applicants have also amended Claim 12 to replace the phrase "saturated or unsaturated heterocyclyl group" in the definition of R_5 and R_6 with the terms "thiophene, pyrrole, imidazole, pyrazole, thiazole, isothiazole, oxazole, isoxazole, pyridine, pyrazine, pyrimidine, pyridazine, pyrrolidine, pyrroline, imidazolidine, imidazoline, piperidine, piperazine, morpholine, tetrahydrofuran, tetrahydropyran, and tetrahydrothiopyran". This amendment is supported by the specification at lines 14-17, page 7. Applicants have further amended Claims 12, 20 and 26 to correct typographical errors. In order to expedite prosecution of the present application, applicants have deleted the non-elected subject matter, i.e., Claims 1-11, 21-25 and 27, and reserve the right to file one or more divisional applications directed to the deleted subject matter.

Since the above amendments do not introduce any new matter into the specification, entry thereof is respectfully requested.

The Abstract of the present application is objected to because it contains more than 150 words.

In response, applicants have submitted a new Abstract to replace the previous Abstract. Applicants further note the new abstract is within the scope of the original disclosure of the present application and does not introduce any new matter into the present application.

The Examiner states that the listing of references in the specification is not a proper information disclosure statement, and thereby requests applicants to submit an Information Disclosure Statement (PTO-892).

Applicants will file the Information Disclosure Statement (PTO-892) once all copies of the references are obtained.

Claims 12-20 and 26 are objected to for informal reasons. More specifically, the Examiner states that the phrase "when R7 is COR'$_{11}$" in Claim 12 appears to be a typographical error and the word "us" in Claim 26 has been misspelled. Thus, the Examiner suggests replacing "R'$_{11}$" in Claim 12 and "us" in Claim 26 with "R_{10}" and "use", respectively. Further, the Examiner suggests making appropriate correction to Claim 20 because the period therein is missing.

Applicants have amended Claims 12, 20 and 26 in accordance with the Examiner's suggestions.

Claims 12-20 and 26 stand rejected under 35 U.S.C. §112, second paragraph, as allegedly indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. More specifically, the Examiner alleges that Claims 12-14 recite improper Markush format.

In response, applicants have amended Claims 12-14 to recite proper Markush format. Applicants respectfully submit that these amendments obviate the rejection under 35 U.S.C. §112, second paragraph.

Claims 12-15 and 26 stand rejected under 35 U.S.C. §102(a) as allegedly anticipated by Thakare, S. S., et al., Asian Journal of Chemistry, Vol. 13, 2001, 237-240 (hereinafter "Thakare et al."). More specifically, the Examiner alleges that the two compounds disclosed at the bottom of page 239 of Thakare et al. (shown below) fall within the scope of formula (I) of Claim 12, and thereby anticipate Claim 12 and the dependent claims thereof.

Claims 12 and 26 also stand rejected under 35 U.S.C. §102(b) as allegedly anticipated by Nawwar, G. A., et al. Archiv der Pharmazie, Vol. 326, 1993, 831-836 (hereinafter "Nawwar, et al.). More specifically, the Examiner alleges that compounds 9a and 9b of Nawwar et al. (shown below) fall within the scope of formula (I) of Claim 12, and thereby anticipate Claims 12 and the dependent claims thereof.

Applicants have amended Claim 12 to remove the compound of formula (I) when R_6 is furan. Applicants submit that Claim 12 and the dependent claims thereof, as amended, are not anticipated by the disclosure of Thakare et al. or Nawwar et al. More specifically, the pyrazoles disclosed in Thakare et al. and Nawwar et al. all have a furan substituent at the 3 position of the pyrazole ring, while the compounds of formula (I), as amended, exclude furan subsitution at the 3 position of the pyrazole ring.

The various §102 rejections have been obviated, thus, reconsideration and withdrawal thereof is respectfully requested.

Claims 12-15, 17-18 and 26 stand rejected under 35 U.S.C. §103(a) as allegedly unpatentable over Thakare et al. in view of Nawwar et al. and Silverman, R. B., The Organic Chemistry of Drug Design and Drug Action, New York, Academic Press, Inc. 1992, pages 19-23 (hereinafter "Silverman"). More specifically, the Examiner alleges that Thakare et al. disclose Claims 12-15 and 26 as stated in the 35 U.S.C. §102(a) rejection, while Silverman and Nawwar

et al. disclose that –CONH– is commonly substituted for –CO– for the purposes of modifying the biological activity of lead compounds, i.e., –CONH– represents a biosteric substitution of –CO–. Thus, the Examiner concludes that it would have been *prima facie* obvious to one skilled in the art to substitute a –CONH– for the –CO– group to arrive at Claims 17-18.

Applicants respectfully submit that Claims 12-15, 17-18 and 26, as amended, are not rendered obvious by the disclosure of Thakare et al. in view of Nawwar et al. and Silverman.

First, the cited references, solely or in combination, fail to teach or suggest the present invention. Thakare et al. disclose certain 2-hydroxy-5-chlorophenyl substituted pyrazole derivatives having herbicidal activity. Nawwar et al. disclose a couple of 2-hydroxy-phenyl substituted pyrazoles among a series of phenyl substituted 3-arylpropenones which have molluscicidal activity. Notably, the pyrazoles disclosed in Thakare et al. and Nawwar et al. all have a furan substituent at the 3 position of the pyrazole ring. However, the compounds of formula (I), as amended, exclude furan subsitution at the 3 position of the pyrazole ring. Silverman discloses that bioisosterism is a lead modification approach that has been shown to be useful to attenuate toxicity or to modify the activity of a lead. However, Silverman does not disclose what groups can be the bioisosteres for a furan ring. Thus, the cited references, solely or in combination, do not teach or suggest a hydroxyaryl pyrazole derivative of formula (I) as claimed in the present application.

Second, there is no simply suggestion available in the cited references which motivates one skilled in the art to modify the pyrazole derivatives of Thakare et al. and Nawwar et al. to arrive at the present invention. The present application is directed to hydroxyaryl pyrazole derivatives of formula (I) as kinase inhibitors and the use thereof in the treatment of diseases caused by and/or associated with an altered protein kinase activity. Thakare et al. relate

to compounds having herbicidal activity, while Nawwar et al. disclose compounds having molluscicidal activity. Neither Thakare et al. nor Nawwar et al. suggest modifying the compounds disclosed therein to obtain kinase inhibitors. Furthermore, Silverman does not disclose or suggests any biosteric substitutions for furan. As discussed previously, the pyrazoles disclosed in Thakare et al. and Nawwar et al. have a furan substituent at the 3 position of the pyrazole ring, while the compounds of formula (I), as amended, exclude furan subsitution at the 3 position of the pyrazole ring. Therefore, applicants submit that one skilled in the art would not be motivated to replace the furan substituent with other groups, particularly in view of the biological activities of the disclosed compounds.

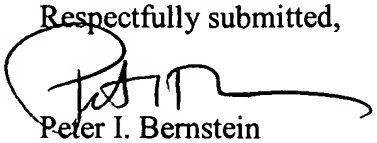
Further, one skilled in the art, in view of the cited references, would not have any reasonable expectation of success in altering the disclosed compounds in such a way as to arrive at the present invention. Silverman discusses the concept of bioisosterism in general terms, but does not teach the specific relationships between the bioisosteres and the biological activity thereof. Particularly, Silverman does not teach how the biological activity of a compound would change if a furan ring and/or a –CO– group are replaced with other groups. Thus, applicants believe that one skilled in the art, in view of the herbicidal and molluscicidal agents of Thakare et al. and Nawwar et al., would not reasonably expect that replacement of the furan ring and/or the –CO– group would result in compounds active as kinase inhibitors as claimed in the present invention.

Accordingly, applicants submit that the Examiner has failed to establish a *prima facie* case of obviousness.

The §103 rejection has been obviated, thus reconsideration and withdrawal thereof are respectfully requested.

In view of the foregoing comments, it is respectfully urged that the Examiner reconsider and withdraw the requirement for restriction and provide an action on the merits with respect to all the claims.

Respectfully submitted,



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